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EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,304	DEL BORGO ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,8,10-23,32,33 and 50-52* is/are pending in the application.

4a) Of the above claim(s) *4,7,8,10-23 and 50-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/19/09 has been entered.

Applicants amendments and arguments filed 5/19/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicants elected with traverse Group I. Since the species was unclear, in an interview (see 4/15/08) it was agreed that the species examined would be the peptide INSL3 (SEQ ID NO:7) as recited in claims 1 and 3 (i.e. no conjugate). The instant claims have been amended. In accord with section 803.02 of the MPEP the examination is extended to the extent necessary to determine patentability of the Markush-type claim.

Claims 2,5-6,9,24-31,34-49 have been cancelled.

Claims 4,7-8,10-23,50-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/13/08.

Claims 1,3,32-33 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

Page 13 line 22 refers to 'anz-halogenated amino acid'. The word 'anz' could not be found in an English dictionary. It appears that there is a spelling or typographical error

Appropriate correction is required.

Claim Rejections - 35 USC § 112

This 112 2nd rejection is a new rejection. As such, applicants arguments are not relevant to the 112 2nd rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3,32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Previously, claim 1 and dependent claims were drawn to 'analogues'. Currently the claims are drawn to peptides that correspond to particular SEQ ID NO's and have modifications. Claim 3 expressly states that the peptide is modified from a particular sequence. However, the scope of the modifications are unclear. As such, the metes and bounds of the claims are unclear.

It is noted that the claims state that the peptides correspond to particular SEQ ID NO's. It is noted that the specification does not provide a specific definition of 'correspond'. A commonly used definition of correspond means 'to be similar' (Correspond definition retrieved from dictionary.com http://dictionary.reference.com/browse/correspond 3 pages, retrieved on

7/27/09). In the instant case, it is unclear how the peptide of the instant claims is 'similar' to the recited SEQ ID NO's. It is unclear if the peptide is similar in size, shape, hydrophobicity, molecular weight, etc. For example, it is unclear if the mere presence of an amino acid is sufficient. Further, claim 3 also suggests that there are modifications from the recited sequences. Although claim 1 refers to modification involving cyclization it is unclear if such modification are the only modifications permissible.

Further, it is noted that claim 1 refers to a halogenated amino acid residue. SEQ ID NO:1-3,7-10 do not include a halogenated amino acid. As such, it is unclear if the halogenated amino acid is inserted somewhere in the sequence or if the halogenated amino acid is substituted for another amino acid. The structure of a peptide in which a halogenated amino acid is inserted is not the equivalent of a sequence in which a halogenated amino acid is substituted for another amino acid. As such, there is more than one reasonable interpretation of the claims.

Claim 1 refers to a spacer group. The possible location of the spacer group is unclear. The claim language runs together and it is unclear if the phrase 'via a spacer group' is intended to refer generally to the covalent bond or specifically to a thioether bond or specifically to a thiother or disulfide bond. As such, there is more than one reasonable interpretation of the claims.

The instant claims refer to positions 2 and 8 and positions 21 and 26 of 'said peptide sequences'. However, the claims refer to 'synthetic monomeric, cyclic B-chain peptide' as well as SEQ ID NO:1 for example. Since SEQ ID NO:1 is not cyclic the 'synthetic monomeric, cyclic B-chain peptide' is not the equivalent of SEQ ID NO:1. It is unclear if 'said peptide sequences' is in reference to the cyclic (or modified) peptide or if 'said peptide sequences' is in reference to

specific SEQ ID NOs. It is noted that if the reference is to the cyclic (or modified) peptide it is unclear if the cyclic portion is numbered and counted clockwise or counterclockwise.

The claims refer to 'disulfide bond between two cysteine residues'. The claims also refer to positions 2 and 8 and 12 and 26. Since SEQ ID NO:1, for example, includes a cysteine residue at position 10, it is unclear if such cysteine can be included in the disulfide bond.

The claims refer to 'monomeric' yet also refer to a cyclic peptide with a spacer. First, it is noted that a peptide is necessarily a polymer unit including repeats of amino acids. Further, 'monomeric' in the context of cyclic peptides is unclear.

Although unclear, for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Since it is unclear if modifications can include insertions, deletions, etc. and it is unclear if the numbering is in reference to a modified or unmodified sequence the claims are given the broadest reasonable interpretation such that any peptide that includes the cyclization modification meets the claim limitations including those which use a naturally present cysteine. Since peptides are necessarily polymeric, such peptides are interpreted as meeting the claim limitations. Further, section 2111.01 I of the MPEP states that the claims should be given the broadest reasonable interpretation in light of the specification. In the instant case, the specification (page 25 lines 27-31, Figure 3 'cINSL3b', claim 51) refer to a specific peptide. The specification states that the peptide is INSL3-based. The sequence of the b-chain of INSL3 is provided by SEQ ID NO:7 and is:

PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Thus SEQ ID NO:7 is 31 amino acids in length. cINSL3b is 27 amino acids in length. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'. Further, SEQ ID NO:7 includes the sequence LCGHH (positions 9-13) while the corresponding sequence in cINSL3b is LSGRH. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'. Although unclear, the claims are currently interpreted as not including any new matter, any future amendments will be analyzed to determine whether or not new matter is present.

Previously, claims were rejected under 112 1st written description. Since claims have been amended an updated rejection appears below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3,32-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that

> "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*,

the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to peptides. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7 Although unclear (see 112 2nd above) for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Since it is unclear if modifications can include insertions, deletions, etc. and it is unclear if the numbering is in reference to a modified or unmodified sequence the claims are given the broadest reasonable interpretation such that any peptide that includes the cyclization modification meets the claim limitations including those which use a naturally present cysteine. Since peptides are necessarily polymeric, such peptides are interpreted as meeting the claim limitations. Further, section 2111.01 I of the MPEP states that the claims should be given the broadest reasonable interpretation in light of the specification. In the instant case, the specification (page 25 lines 27-31, Figure 3 'cINSL3b', claim 51) refer to a specific peptide. The specification states that the peptide is INSL3-based. The sequence of the b-chain of INSL3 is provided by SEQ ID NO:7 and is:
PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Thus SEQ ID NO:7 is 31 amino acids in length. cINSL3b is 27 amino acids in length. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'. Further, SEQ ID NO:7 includes the sequence LCGHH (positions 9-13) while the corresponding sequence in cINSL3b is LSGRH. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high. However, the ability to predict any and all sequences that bind to a biological target of the relaxin superfamily protein and modulate an activity of the biological target is limited.

(2) Partial structure:

In the instant case, the claims are drawn to peptides. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7 Although unclear (see 112 2nd above) for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Thus as long as a cyclic modification is present any amount of modifications, substitutions is permissible.

In considering the possible variability, if SEQ ID NO:7 (31 amino acids) was substituted at every position except for the cysteine residues with any of the 20 natural amino acids (i.e. an analog) there would be 20^{29} (i.e. 536870912000000000000000000000000000) possible analogues. If there are substitutions with alkylmalonyl groups as discussed in section 0072 or if fusion compounds are considered the variability further increases. Hence, there is substantial variability in the genus.

Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible peptides). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ

ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages from positions 2-3 and disulfide bonds. There appear to be no examples based on SEQ ID NO:8-9 for example.

Since there are a substantial variety of peptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 states that the peptides bind a biological target of the relaxin superfamily protein and modulate an activity of the biological target.

However, there is no disclosed correlation between structure and function for all of the peptides. It is noted that claim 3 recites a particular sequence but the claim is drawn to a peptide modified from that sequence. As such, there is no common core sequence. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind a biological target. Although the claims refer to cross-links between positions 2 and 8 and 21 and 26 there is no teaching for the different sequences relating to the function of such residues. In particular, no common core sequence is taught. One of skill in the art would

reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention:

The specification (specifically example 1) describes the solid-phase synthesis of peptides, however the specification fail to describe the synthesis of a representative number of peptides. Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible analogues). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages from positions 2-3 and disulfide bonds.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,3,32-33 is/are broad and generic, with respect to all possible peptides encompassed by the claims. The possible structural variations are many. Although the claims may recite some

functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the peptides beyond those peptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of peptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of peptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments 112 written description

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the claims recite modification of only 7 discrete starting molecules. Applicants argue that examples are provided.

Applicant's arguments filed 5/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that the claims recite modification of only 7 discrete starting molecules, as discussed above the claims and thus the extent of the modifications is unclear. If the type and number of modifications are limitless it does not matter if the starting molecules are 7 discrete molecules or 1 discrete molecule.

Although Applicants argue that examples are provided, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible peptides as discussed above). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages from positions 2-3 and disulfide bonds.

Claim Rejections - 35 USC § 101

Claims were previously rejected under 101. Since the claim have been amended an updated rejection appears below.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1,3,32-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

As discussed below, Schwabe et al. (US 5,911,997; first cited with office action 4/15/08) teach (Figure 1 and Figure 1 caption column 3 lines 43-49; claim 1) a peptide identified as the relaxin-like factor (RLF). The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTEA) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. As shown in Figure 1 of Schwabe the B-chain of RLF is linked with the A-chain of RLF. In particular, residue 10 (i.e. Cys) and residue 22 (i.e. Cys) of the B-chain are linked to the A-chain. Together, residues 10-22 of the B chain of RLF form a cyclic structure with residues 11-24 of the A chain of RLF. In other words the sequence of the cyclic structure includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC). Schwabe teach compositions of RLF (column 3 line 7-12) and teach pharmaceutical compositions of RLF with carriers for example (column 8 lines 37-55) as recited in claim 32-33 of the instant invention.

Although unclear, for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Since it is unclear if modifications can include insertions, deletions, etc. and it is unclear if the numbering is in reference to a modified or unmodified sequence the claims are given the broadest reasonable interpretation such that any peptide that includes the cyclization modification meets the claim limitations including those

which use a naturally present cysteine. Since peptides are necessarily polymeric, such peptides are interpreted as meeting the claim limitations. Further, section 2111.01 I of the MPEP states that the claims should be given the broadest reasonable interpretation in light of the specification. In the instant case, the specification (page 25 lines 27-31, Figure 3 'cINSL3b', claim 51) refer to a specific peptide. The specification states that the peptide is INSL3-based. The sequence of the b-chain of INSL3 is provided by SEQ ID NO:7 and is: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Thus SEQ ID NO:7 is 31 amino acids in length. cINSL3b is 27 amino acids in length. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'. Further, SEQ ID NO:7 includes the sequence LCGHH (positions 9-13) while the corresponding sequence in cINSL3b is LSGRH. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'.

It is noted that claim 1 recites a cyclic peptide. As discussed above, Schwabe teach a cyclic structure that includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC) (Figure 1), thus the peptide is cyclic. The peptide of Schwabe is of SEQ ID NO:7 (a linear peptide) with a cyclic modification since the peptide of Schwabe includes disulfide bonds and cyclization thus meeting the limitations of claims 1,3 of the instant invention. It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can not have mutually exclusive properties. In the instant case, the peptide of Schwabe meet the claim limitations so the peptide necessarily has the claimed activity. Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is

from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50) thus the peptide is synthesized in nature.

Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50). There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature. It is noted that the instant claims refer to 'synthetic'. However, by definition 'synthetic' refers to something that has been synthesized. Since Schwabe teach that the relaxin-like factor is a naturally occurring peptide it has been synthesized by a natural process and thus is 'synthetic'.

Response to Arguments 101

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the word 'synthetic' is used in the claims.

Applicant's arguments filed 5/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that the word 'synthetic' is used in the claims, by definition 'synthetic' refers to something that has been synthesized. Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50). Since Schwabe teach that the relaxin-like factor is a naturally occurring peptide it has been synthesized by a natural process and thus is 'synthetic'. Further, "synthetic" does not imply non-naturally occurring. Synthetic implies a mode of

making a peptide. A naturally occurring peptide made synthetically would still be a product of nature. There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment.

Claim Rejections - 35 USC § 102

Previously, claims were rejected under 102b using the Schwabe reference cited below. Since claims have been amended an updated rejection appears below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3,32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwabe et al. (US 5,911,997; first cited with office action 4/15/08).

Schwabe et al. (US 5,911,997) teach (Figure 1 and Figure 1 caption column 3 lines 43-49; claim 1) a peptide identified as the relaxin-like factor (RLF). The peptide includes the B-chain portion identified as SEQ ID NO:4 (i.e. PTPEMREKLCGHHFVRALVRVCGGPRWSTEA) which includes the primary sequence (without the disulfide bonds) identified as SEQ ID NO:7 of the instant invention. As shown in Figure 1 of Schwabe the B-chain of RLF is linked with the A-chain of RLF. In particular, residue 10 (i.e. Cys) and residue 22 (i.e. Cys) of the B-chain are linked to the A-chain. Together,

residues 10-22 of the B chain of RLF form a cyclic structure with residues 11-24 of the A chain of RLF. In other words the sequence of the cyclic structure includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC). Schwabe teach compositions of RLF (column 3 line 7-12) and teach pharmaceutical compositions of RLF with carriers for example (column 8 lines 37-55) as recited in claim 32-33 of the instant invention.

Although unclear, for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Since it is unclear if modifications can include insertions, deletions, etc. and it is unclear if the numbering is in reference to a modified or unmodified sequence the claims are given the broadest reasonable interpretation such that any peptide that includes the cyclization modification meets the claim limitations including those which use a naturally present cysteine. In the instant case, Schwabe teach Cys residues crosslinked to form a cyclic peptide (Figure 1). Since peptides are necessarily polymeric, such peptides are interpreted as meeting the claim limitations. Further, section 2111.01 I of the MPEP states that the claims should be given the broadest reasonable interpretation in light of the specification. In the instant case, the specification (page 25 lines 27-31, Figure 3 'cINSL3b', claim 51) refer to a specific peptide. The specification states that the peptide is INSL3-based. The sequence of the b-chain of INSL3 is provided by SEQ ID NO:7 and is: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Thus SEQ ID NO:7 is 31 amino acids in length. cINSL3b is 27 amino acids in length. Thus it is consistent with the specification that

'correspond to' is not the equivalent of 'identical to'. Further, SEQ ID NO:7 includes the sequence LCGHH (positions 9-13) while the corresponding sequence in cINSL3b is LSGRH. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'.

It is noted that claim 1 recites a cyclic peptide. As discussed above, Schwabe teach a cyclic structure that includes residues 10-22 of the B chain of RLF followed by residues 24-11 of the A chain of RLF (i.e. CGHHFVRALVRVCCLTLLDQQTCGSLC) (Figure 1), thus the peptide is cyclic. The peptide of Schwabe is of SEQ ID NO:7 (a linear peptide) with a cyclic modification since the peptide of Schwabe includes disulfide bonds and cyclization thus meeting the limitations of claims 1,3 of the instant invention. It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can not have mutually exclusive properties. In the instant case, the peptide of Schwabe meet the claim limitations so the peptide necessarily has the claimed activity. Schwabe teach that the relaxin-like factor (for example as shown in Figure 1) is from a human source (human Ley I-L) (column 3 lines 7-12 and column 2 lines 26-50) thus the peptide is synthesized in nature.

Response to Arguments 102 Schwabe

Since the claims have been amended, a new rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue that the claims refer to a monomer and a dimer is defined as a molecule which consists of subunits.

Applicant's arguments filed 5/19/09 have been fully considered but they are not persuasive.

Although Applicants argue that the claims refer to a monomer and a dimer is defined as a molecule which consists of subunits, as discussed above the claims are unclear. First, it is noted that a peptide is necessarily a polymer unit including subunits of amino acids. The instant specification provides no specific definition of 'monomeric'. There is no definition provided in the instant specification of 'monomeric' in the context of cyclic peptides. Thus the peptides as claimed can not be monomeric based on the applicants cited definition. Since a peptide is necessarily a polymer unit including subunits of amino acids, applicants cited definition is evidence that the claims are unclear and confusing. Further, 'monomeric' in the context of cyclic peptides or disulfide bonded peptides is unclear. Further, it is noted that the claims refer to 'spacer groups'. When the cross-link is connected via a spacer that is a sequence of amino acids, it is unclear what differentiates a cyclic monomeric peptide from a cyclic dimeric peptide from a cyclic peptide.

This rejection is a new rejection.

Claims 1,3,32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bullesbach et al. (Chem Pept Proteins Proc 1982 pages 327-335, cited in IDS 8/7/08 as cite AD).

Bullesbach teach the preparation of the B-chain of an insulin peptide (Figure 2, page 328 last paragraph) in which the cysteine residues at positions 7 and 19 are cross-linked. Since Bullesbach teach that the peptide was prepared it was necessarily present in a composition as recited in claims 32-33.

Although unclear, for purposes of examination the claims are given the broadest reasonable interpretation. Since the claims state that the peptide 'corresponds' to particular sequences and the definition of correspond is 'similar', any similarity (the presence of amino acids, for example) is deemed sufficient to 'correspond'. Since it is unclear if modifications can include insertions, deletions, etc. and it is unclear if the numbering is in reference to a modified or unmodified sequence the claims are given the broadest reasonable interpretation such that any peptide that includes the cyclization modification meets the claim limitations including those which use a naturally present cysteine. Bullesbach specifically show a cross-link between amino acids (Figure 2). Since peptides are necessarily polymeric, such peptides are interpreted as meeting the claim limitations. Further, section 2111.01 I of the MPEP states that the claims should be given the broadest reasonable interpretation in light of the specification. In the instant case, the specification (page 25 lines 27-31, Figure 3 'cINSL3b', claim 51) refer to a specific peptide. The specification states that the peptide is INSL3-based. The sequence of the b-chain of INSL3 is provided by SEQ ID NO:7 and is:
PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. Thus SEQ ID NO:7 is 31 amino acids in length. cINSL3b is 27 amino acids in length. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'. Further, SEQ ID NO:7 includes the sequence LCGHH (positions 9-13) while the corresponding sequence in cINSL3b is LSGRH. Thus it is consistent with the specification that 'correspond to' is not the equivalent of 'identical to'.

It is noted that claim 1 states that the peptide modulates an activity of the biological target. Section 2112.01 of the MPEP states that products of identical chemical compositions can

not have mutually exclusive properties. In the instant case, the peptide of Bullesbach meet the claim limitations so the peptide necessarily has the claimed activity.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654